D YOUNG & CO
INTELLECTUAL
PROPERTY

European Biotech Case Law Webinar

21 September 2021

Speakers

Simon O'Brien
Partner, Patent Attorney
swo@dyoung.com

Antony Latham
Senior Associate, Patent Attorney
aml@dyoung.com

Agenda

- T966/18 (Prothena Biosciences Limited) – when does preclinical data plausibly support a therapeutic effect?
- T799/16 (Acorda Therapeutics, Inc.) – dosage regimes – navigating the sufficiency and inventive step requirements
- T0096/20 (Alexion Pharmaceuticals, Inc.) – clinical trial protocols as prior art
- T116/18 (Sumitomo Chemical Company) – referral to EBA regarding when post-published data can be taken into account for inventive step
- G1/21 – when can an appeal board order oral proceedings by ViCo?
- G4/19 – double-patenting

T966/18 (Prothena Biosciences Limited) – when does preclinical data plausibly support a therapeutic effect?

Background

- EP1578253 relates to antibodies for the treatment of Lewy body disease, in particular the use of the anti-α-synuclein (α-SN) antibody Prasinezumab
- OD considered the MR to add matter and AR1 filed during OPs to lack sufficiency
- Appeal: claims corresponding to AR1 of opposition OPs

Claim 1 on Appeal

- "1. A pharmaceutical composition comprising an agent that induces an immunogenic response against α-synuclein, for use in prophylaxis or treatment of a disease characterized by Lewy bodies or α-synuclein aggregation in the brain, wherein the agent is α-synuclein or an immunogenic fragment thereof or an antibody to α-synuclein or an immunogenic fragment thereof, and wherein the disease is Parkinson's disease, dementia with Lewy bodies, diffuse Lewy body disease, pure autonomic failure, Lewy body dysphagia, incidental Lewy body disease, inherited Lewy body disease or multiple system atrophy."

Prior art

- α-SN aggregation was known to be linked to Lewy body disease (D50-53)
  - but according to OD, no accepted relationship to cause of disease was known
- Reduction in α-SN aggregation had been achieved by α-SN-binding peptides and antibodies (D1; D2)
- Vaccination with α-SN resulted in antibody titres
  - but an effect on aggregates was not measured (D30)

Data in the patent

- Mouse model of Lewy Body disease
  - treated with α-SN (low titre, high titre) or no α-SN (control)
  - α-SN Ab titre in the brain tissue was measured

Data in the patent

Table 1

Group	Genotype	n=	Age at Sac	Treatment/Length	Titers	Syn (+) inclusions/ mm2
I	Syn Tg	4	10-13 mo	a-syn+CFA 50ug/inj for 3mo sac'd 3mo later	2,000-8,000	15-29
II	Syn Tg	4	10-13 mo	a-syn+CFA 50ug/inj for 3mo sac'd 3mo later	12,000-30,000	10-22
III	Syn Tg	4	10-13 mo	PBS+CFA for 3mo sac'd 3mo later	0	18-29

Data in the patent

- Board: Correlation between Ab titre and reduction in α-SN aggregates
  - i.e. administration with α-SN elicits production of α-SN antibodies
- Passive immunisation: only *in vitro* binding measured

Later published evidence

- Patentee further submitted post-published data from clinical trials
  - phase 2 clinical trial (NCT03100149) for Prasinezumab showing a clinical effect (D91).
- Board considered that the quantitative data in the application as filed, in combination with the CGK were enough to plausibly demonstrate an effect without recourse to the later published evidence.

Decision

- BoA considered that:
- In view of the body of prior art, the skilled person was aware of a link between the reduction in α-SN aggregation and the treatment of Lewy Body Disease.
  - this contrasted with the OD's view
- Prior art relied on by the OD actually strengthened the view that α-SN is causative for Lewy Body Disease.

Decision

- The data need to be seen against the background of the skilled person's understanding of the prior art i.e. that reduction of aggregates is an accepted measure of likely therapeutic effects on Lewy Body Disease
  - The data is in line with the expectation based on the prior art.
- From the combined qualitative and quantitative data the skilled person would have concluded that the patent shows that active immunisation results in antibodies which cross the BBB and reduce α-SN aggregates
- Thus it is also plausible that passive immunisation would achieve a similar effect
- Remitted to OD - who had **not** considered priority, novelty and inventive step

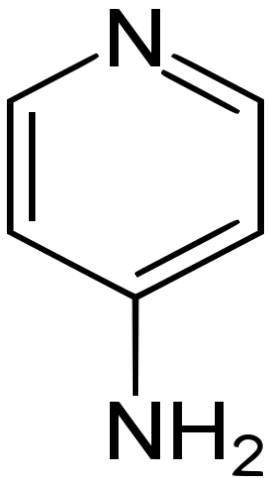
Discussion points

- Even though the patentee did not need to rely on it, would the outcome have been different if the later clinical trial data had not been available?
- Prior art lowers the bar for data requirement in the application – what is the impact on inventive step?
  - Recent decision T 33/19 may shed some light.

T799/16 (Acorda Therapeutics, Inc.) – dosage regimes: walking the fine line between insufficiency and obviousness

Fampyra/4-aminopyridine

- Potassium channel blocker
- Marketed as Fampyra in EU for management of certain symptoms of MS



EP 2377536 – independent claims

- 1. A sustained release 4-aminopyridine composition for use in a method of increasing walking speed of a patient with multiple sclerosis, wherein said composition is administered twice daily in a dose of 10 milligrams of 4-aminopyridine.

- 5. Use of 4-aminopyridine in the manufacture of a sustained release composition for increasing walking speed in a patient with multiple sclerosis, wherein said composition is administered twice daily in a dose of 10 milligrams of 4-aminopyridine.

Sufficiency

- Further medical use – therapeutic efficacy of composition *and dosage* must be credible to meet requirement of Article 83 EPC
- Sufficiency of disclosure of composition not disputed

Sufficiency and ‘non-responders’

- Only about one third of patients response to 4-aminopyridine
- Fact not disputed – acknowledged in application as filed and evident from Examples
  - Developed a “responder analysis”

Sufficiency and ‘non-responders’

- Opponents argued use of 4-aminopyridine at a dose of 10 mg twice daily was not sufficiently disclosed across the whole scope of the claim
- Patentee argued that subpopulations of non-responders were common for many treatments

- Contrary to the respondents' view, the existence of non-responders is not a reason to deny sufficiency of disclosure, and the treatment of non-responders does not have to be excluded or disclaimed.

- The existence of a substantial proportion of patients who are non-responders is a common phenomenon observed with drugs in many treatment areas, such as diabetes, migraine or cancer. It is common practice to treat patients with a drug and change their medication should it turn out that they do not respond to the treatment.

- If it can be shown that a relevant proportion of patients benefits from a treatment and that it has acceptable safety, the criterion of sufficiency of disclosure is met, since the person skilled in the art has the necessary technical information to perform the treatment.

Comparison with UK case law

- *Warner Lambert v Actavis*
- Use of pregabalin to treat neuropathic pain insufficient.
- Lord Sumption: specification did not plausibly demonstrate that drug would treat all types of pain.
- Pain can be caused by a number of different underlying mechanisms, and pregabalin was only demonstrated in the patent application as filed as targeting one of these mechanisms.

Inventive step: “obvious-to-try”

- New dosage regimes often dismissed as lacking inventive step – obvious to run clinical trials to determine optimal dose of known drug

Closest prior art

- C27 – financial statement reporting results of Phase II trial to determine optimal dose in MS patients
- Doses in range 10 to 25 mg b.i.d. improved walking speed in MS patients
- Larger Phase III trial initiated to compare doses of 10, 15, and 25 mg b.i.d.
- **Difference** between invention and CPA was efficacy of 10 mg b.i.d. dosage regime for increasing walking speed of MS patients

Opponent's arguments

- Argued in view of CPA:
  - Skilled person would be motivated to find lowest effective dose;
  - Given disclosure of Phase III trial underway – reasonable expectation of success that dose would be effective; and
  - Setting up clinical trial would be routine for skilled person.

- "…presumably due to the **high intra-patient and inter-patient variability of disease symptoms** (here walking speed) in the case of MS and the relatively high proportion of non-responders to 4-aminopyridine, it actually turned out to be **exceptionally difficult** in this case to provide the required proof of efficacy - as shown in [the examples and Declaration C20]. The MS-F202 study provides experimental evidence of this difficulty."

- “using conventional methods, the person skilled in the art would have thus failed to appreciate the utility of the 10 mg bid dosage regime”

Summary

- Rare case of dosage regime claim surviving sufficiency and ‘obvious-to-try’ attacks
- Critical factor appears to be complexity and likelihood of success of clinical trials in the disease in question, i.e. MS
- Perceived difficulties in setting up a clinical trial could help your case

T0096/20 (Alexion Pharmaceuticals, Inc.) – clinical trial protocols as prior art

Background

- Application directed to anti-C5 antibody for the treatment of neuromuscular disorder myasthenia gravis (MG)
- ED refused application as lacking inventive step in view of D4
- D4 discloses the set-up of a **phase II clinical trial** to determine safety and efficacy of an anti-C5 antibody

Case Law

- **Novelty recognised** for medical use claims over prior art disclosures indicating that clinical trials were underway, but whose results were not yet reported (e.g. T 158/96, T 715/03 and T 385/07)
- **Inventive step bar** - therapeutic is undergoing clinical trials but results of the trial have not been made available to the public (e.g. T 239/16 and T 2506/12)

T 239/16

- Phase II clinical trial protocol may provide a reasonable expectation of success
- Reasonable expectation of success arises because **clinical trials are known to be based on earlier preclinical studies** (thereby suggesting the success of the therapeutic concerned) and because their approval entails ethical considerations which require that a benefit will arise with "reasonable certainty“.
- Active agent generally known to be effective in treating the condition

T 2506/12

- Clinical phase I study assessing the combination treatment of cancer
- “drug compounds to be used in a clinical trial with human subjects are not selected based on a general "try-and-see" attitude, but based on existing favourable scientific data, for both ethical and economical reasons. Thus a clinical trial is **not a mere screening exercise**.”
- “combination looked **promising in terms of efficacy** - safety had yet to be assessed but “no particular reason was known which would have discouraged the person skilled in the art from carrying out an experimental evaluation”

Summary of P's arguments

- Clinical trial (D4) did not provide a reasonable expectation of success that MG could be treated with an anti-C5 antibody:
  - targeting the complement system did not inevitably result in treatment of a complement-associated disorder
  - various unsuccessful attempts to target complement factors in different diseases
  - MG difficult to treat – **no therapy approved >60 years**

Summary of BoA decision (continued)

- Such a clinical trial provides a reasonable expectation of success – unless there is evidence to contrary
- Mere fact no MG therapy approved for long time does not diminish expectation of success
- Failure of other complement-inhibitors to treat diseases unrelated to MG did not diminish expectation of success
- Only evidence relating to the **same** compound and **same** disease would be suitable

Summary

- Clinical trial protocols very relevant to inventive step
- The presumption of a reasonable expectation of success must be rebutted e.g. by providing evidence calling into question the efficacy of the therapy
- Timing is crucial – therapy must be at least “plausible” but also inventive

T116/18 (Sumitomo Chemical Company) – when can post-published data can be taken into account for inventive step?

Background

- EP2484209 - Granted claim 1 relates to an insecticide composition comprising a combination of two (or more) compounds, namely thiamethoxam and at least one compound represented by a genus.
- Inventive step - patentee argued that this combination of compounds provides a ***surprising synergistic effect***.
- Application - contains data showing that ***two specific compounds*** from the genus, in combination with thiamethoxam, ***provide a synergistic effect***.

Filing of post-published data

- Opponent – data not enough to make it plausible that synergistic effect achieved across whole claim scope, e.g. due to breath of genus
- Patentee – filed its own post-published data showing that other combinations provide a synergistic effect
- Opponent – post-published data cannot be relied on, not plausible the effect achieved across claim scope at FD

Divergence of case law

- Post published data supporting technical effect can only be taken into account if the effect was already plausible at the filing date (T448/16, T1329/04 and T433/05)
- Not consistent with other case law such as: T1422/12; T2371/13 and T31/18
- Who must show plausibility (or lack of plausibility)? T1329/04 patentee's burden; T184/16 opponent's burden

Provisional questions

If for acknowledgement of inventive step the patent proprietor relies on a technical effect and has submitted data or other evidence to prove such effect, ***such data or other evidence having been generated only after the priority or filing date of the patent*** *(post-published data):*

1. Should an exception to the principle of free evaluation of evidence (see e.g. G 1/12 reasons 31) be accepted in that the post-published data must be disregarded on the ground that the proof of the effect rests ***exclusively*** *on such post-published data?*

Provisional questions (continued)

2. If the answer is yes (post published data must be disregarded if the proof of the effect rests exclusively on these data): can post-published data be taken into consideration if based on the information in the patent application ***the skilled person at the relevant date would have considered the effect plausible*** *(ab initio plausibility)?*

3. If the answer to the first question is yes (post published data must be disregarded if the proof of the effect rests exclusively on these data): can post-published data be taken into consideration if based on the information in the patent application ***the skilled person at the relevant date would have seen no reason to consider the effect implausible*** *(ab initio implausibility)?*

G1/2 – when can an appeal board order oral proceedings by ViCo?

Background

- On 15 December 2020:

  From 1 January 2021 BoA may conduct oral proceedings by **VICO even without the agreement of the parties** concerned, as has now been made clear in the **new Article 15a RPBA** adopted by the Boards of Appeal Committee. Since the new provision **merely clarifies** an existing possibility, boards may adapt their practice as regards dispensing with the need to obtain the agreement of the parties concerned even before the date of its entry into force.

- From 1 January 2021:

  Some OPs before BoA, ED, OD conducted by vico **without the consent** of the parties

- Referral from T1807/15

*“Is the conduct of oral proceedings in the form of a **videoconference** compatible with the right to oral proceedings as enshrined in **Article 116(1)** EPC if **not all** of the parties to the proceedings have given their **consent** to the conduct of oral proceedings in the form of a videoconference?”*

Order issued by Enlarged BoA

*"During a **general emergency** impairing the parties' possibilities to attend in-person oral proceedings at the EPO premises, the conduct of oral proceedings before the **Boards of Appeal** in the form of a videoconference is compatible with the EPC even if not all of the parties to the proceedings have given their consent to the conduct of oral proceedings in the form of a videoconference."*

Questions unanswered

- What constitutes “period of general emergency”?
- Can OPs by ViCo be held without the consent of the parties **in the absence** of a period of general emergency?
- Can OPs by ViCo be held without the consent of the parties in **examination** or **opposition** proceedings before the EPO's departments of first instance?

G4/19 – double-patenting

Background

- There is no specific provision in the EPC that prohibits double patenting
- The EPO had previously concluded that an applicant has no **legitimate interest** in obtaining two patents for the same invention.
- What constitutes the “same invention”?

Questions

*1) **Can a European patent application be refused under Article 97(2) EPC** if it claims the same subject-matter as a European patent which was granted to the same applicant and does not form part of the state of the art pursuant to Article 54(2) and (3) EPC?*

Questions (continued)

*2.1) If the answer to the first question is yes, **what are the conditions for such a refusal**, and are different conditions to be applied depending on whether the European patent application under examination was filed*

*a) **on the same date** as, or*

*b) as a European **divisional application** (Article 76(1) EPC) in respect of, or*

*c) **claiming the priority** (Article 88 EPC) in respect of a European patent application on the basis of which a European patent was granted to the same applicant?*

*2.2) In particular, in the last of these cases, does an applicant have a **legitimate interest** in the grant of a patent on the (subsequent) European patent application in view of the fact that the filing date and not the priority date is the relevant date for calculating the term of the European patent under Article 63(1) EPC?*

"1. A European patent application ***can be refused under Articles 97(2) and 125 EPC*** *if it claims the same subject-matter as a European patent which has been granted to the same applicant and does not form part of the state of the art pursuant to Article 54(2) and (3) EPC.*

2.1 The application can be refused on that legal basis, irrespective of whether it

a) was filed ***on the same date*** *as, or*

b) is an earlier application or a ***divisional application*** *(Article 76(1) EPC) in respect of, or*

c) claims the ***same priority*** *(Article 88 EPC) as the European patent application leading to the European patent already granted."*

Consequences and unanswered questions

- Practice of prosecuting both priority and later application should not be pursued despite “legitimate interest”
- What constitutes the “**same invention**”?
- What constitutes the “same applicant”?

*The technical boards have several times considered the notion of the "same subject-matter". **A mere (partial) overlap does not prejudice the grant of a patent** (see T 587/98, OJ 2000, 497; T 877/06; T 1491/06; T 1391/07; T 2402/10; T 2461/10; T 1780/12; T 621/15). See in this chapter II.F.5.2. On the relevance of the scope of protection for the issue of double patenting, see e.g. T 1780/12 and T 2563/11.*

T 1391/07

- The practice of prohibition of "double patenting" is confined to claims conferring notionally the **same scope of protection**.
- The lack of legitimate interest cannot be invoked when the scopes of protection conferred by the respective subject-matters **overlap only partially** with each other.

Conclusion

- Double patenting objections are unlikely to arise provided that the claims in question can be shown to have **non-identical scope**
- A mere difference in wording of claims is unlikely to suffice
- A mere difference in description is unlikely to suffice (see T 2563/11)

Further Information

Training, conferences, workshops, seminars & webinars.

Patent and trade mark newsletters, articles and updates, case law books.

Sign up by email to subscriptions@dyoung.com

Follow us on LinkedIn
www.linkedin.com/company/d-young-&-co-llp

Follow us on twitter
dyoungip

Any Questions…?

Simon O'Brien
Partner, Patent Attorney
swo@dyoung.com

Antony Latham
Senior Associate, Patent Attorney
aml@dyoung.com